(8) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[42 FR 59858, Nov. 22, 1977, as amended at 45 FR 16472, Mar. 14, 1980; 49 FR 6092, Feb. 17, 1984; 50 FR 19918, 19919, May 13, 1985]

§ 440.71 Penicillin V.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Penicillin V is 3,3-dimethyl - 7-oxo-6-(2-phenoxyacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid. It is so purified and dried that:

(i) Its potency is not less than 1,525 units nor more than 1,780 units per milligram.

(ii) [Reserved]

(iii) Its moisture content is not more than 2.0 percent.

(iv) Its pH in a saturated aqueous solution is not less than 2.5 and not more than 4.0.

(v) Its penicillin V content is not less than 90 percent and not more than 105 percent.

(vi) It is crystalline.

(2) *Labeling.* In addition to the labeling requirements of § 432.5 of this chapter, each package shall bear on its outside wrapper or container and the immediate container the statement ''For use in the manufacture of nonparenteral drugs only.''

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, penicillin V content, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*— (1) *Potency.* Assay for potency by any of the following methods; however, the results obtained from the bioassay method shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample (approximately 30 milligrams) in 2.0 milliliters of absolute methyl alcohol. Further dilute an aliquot of this solution with sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to the reference concentration of 1.0 unit of penicillin V per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 436.205 of this chapter.

(2) [Reserved]

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using a saturated aqueous solution prepared by adding approximately 30 milligrams per milliliter.

(5) *Penicillin V content.* Accurately weigh approximately 20 milligrams of the sample, dissolve in absolute methanol, and make to 100 milliliters with absolute methyl alcohol. Treat a portion of the working standard in the same manner. Using a suitable spectrophotometer equipped with a quartz cell and absolute methyl alcohol as the blank, determine the absorbance of the peak at 276 nanometers. Calculate the percent penicillin V as follows:

$$\text{Percent penicillin V} = \frac{\text{Absorbance of sample} \times \text{weight in milligrams of standard} \times \text{Percent penicillin V in standard}}{\text{Absorbance of standard} \times \text{Weight in milligrams of sample}}$$

(6) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[42 FR 59859, Nov. 22, 1977, as amended at 50 FR 19918, 19919, May 13, 1985]

§ 440.73 Penicillin V potassium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Penicillin V potassium is the potassium salt of 3,3-dimethyl-7-oxo-6-(2-phenoxyacetamido) - 4 -thia - 1

- azabicyclo[3.2.0]heptane - 2 - carboxylic acid. It is so purified and dried that:

(i) Its potency is not less than 1,380 units nor more than 1,610 units per milligram.

(ii) [Reserved]

(iii) Its loss on drying is not more than 1.5 percent.

(iv) Its pH in an aqueous solution containing 30 milligrams per milliliter is not less than 4.0 and not more than 7.5.

(v) Its penicillin V content is not less than 81.2 percent and not more than 94.7 percent.

(vi) It is crystalline.

(2) *Labeling.* In addition to the labeling requirements of § 432.5 of this chapter, each package shall bear on its outside wrapper or container and the immediate container the statement ''For use in the manufacture of nonparental drugs only.''

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, loss on drying, pH, penicillin V content, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Assay for potency by any of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 1.0 unit of penicillin V per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 436.205 of this chapter.

(2) [Reserved]

(3) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 30 milligrams per milliliter.

(5) *Penicillin V content.* Dissolve and dilute approximately 20 milligrams of the sample, accurately weighed to 100 milliliters with 0.1*N* sodium hydroxide solution. Treat a portion of the penicillin V working standard in the same manner. Using a suitable spectrophotometer equipped with a quartz cell and 0.1*N* sodium hydroxide solution as the blank, determine the absorbance of the peak at 275 nanometers. Calculate the percent penicillin V as follows:

$$\text{Percent penicillin V} = \frac{\text{Absorbance of sample} \times \text{Weight in milligrams of standard} \times \text{Percent penicillin V in standard}}{\text{Absorbance of standard} \times \text{Weight in milligrams of sample}}$$

(6) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[42 FR 59859, Nov. 22, 1977, as amended at 50 FR 19918, 19919, May 13, 1985]

§ 440.74a Sterile penicillin G procaine.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Penicillin G procaine is 3,3 - dimethyl - 7 - oxo - 6 - (2 - phenylacetamido) - 4 - thia - 1 - azabicyclo [3.2.0]heptane-2-carboxylic acid 2-(diethylamino) ethyl *p*-aminobenzoate compound (1:1). It is so purified and dried that:

(i) Its potency is not less than 900 units and not more than 1,050 units per milligram.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]